affinity for differing binding partners that can be measured using flow cytometry." The Examiner also alleged that "it would be obvious to use a label or package insert to list the contents of said composition." Applicant respectfully traverses.

The '180 patent does not disclose a kit that includes a solid phase reagent, the solid phase reagent comprising a particle coated with capture antibodies having specific binding affinities for member A of the binding pair, wherein substantially all the capture antibodies are oriented on the particle such that the antigen binding regions of the capture antibodies are available for binding member A of the binding pair; first antibodies having specific binding affinities for member A of the binding pair, wherein the first antibodies are labeled with a first label; and second antibodies having specific binding affinities for member B of the binding pair, wherein the second antibodies are labeled with a second label.

The '180 patent discloses sets of beads that have identical light scatter characteristics (forward light scatter, side light scatter, fluorescent emission in at least one wavelength, and preferably two wavelengths). See, the '180 patent, column 4, lines 4-17. The beads can be labeled with two or more fluorochromes such as a red fluorochrome and an orange fluorochrome. See, the '180 patent, column 4, lines 61-67. Each bead set that is used incorporates varying amounts of fluorescent dyes. Detection of the captured analyte is performed with a single fluorescently labeled antibody, such as a fluoroscein labeled antibody, that has an emission that is distinct from the dyes incorporated into the beads. See, the '180 patent, column 4, line 67 through column 5, line 2. Although multiple antibodies may be used to detect captured analyte, each of the antibodies is labeled with the same fluorescent molecule. Thus, the assay described in the '180 patent is able to assess only one analyte per bead. In contrast, the kit of claims 20 and 21 includes two antibodies that are labeled differently, allowing both members of a binding pair to be measured simultaneously. Thus, the '180 patent does not disclose a kit as recited in claims 20 and 21. Furthermore, the '180 patent does not teach or suggest such kits. In view of the above remarks, the Examiner is requested to withdraw the rejection of claims 20 and 21.

Rejection under 35 U.S.C. §103

The Examiner rejected claims 1-21 under 35 U.S.C. §103 over Kortright et al. (U.S. Patent No. 4,870,003, the'003 patent) in view of Jackson et al. (U.S. Patent No. 5,776,709, the '709 patent). The '003 patent was deemed to disclose a solid-phase immunoassay for the simultaneous detection of both members of a binding pair in physiological fluid. The Examiner alleged that the '003 patent disclosed methods "consisting of coating a solid phase reagent with a capture antibody (anti-HIV monoclonal antibody); exposing said solid phase reagent to a biological sample to bind one member of the binding pair; and adding labeled antibodies to detect the levels of each member of the binding pair." The '709 patent was deemed to disclose use of fluorescently labeled antibodies and methods for using multiple stains simultaneously in flow cytometry, as well as the benefit of using multiple fluorescent labels. Applicant respectfully traverses.

Independent claim 1 relates to a method for simultaneously measuring both members A and B of a binding pair in a biological sample. The method includes

a) providing a solid phase reagent, the solid phase reagent comprising a particle coated with capture antibodies having specific binding affinities for member A of the binding pair;

b) contacting the biological sample with the solid phase reagent under conditions in which member A, if present, becomes bound to the particle, to form a first reacted particle;

c) contacting the first reacted particle with first antibodies having specific binding affinities for member A, wherein the first antibodies are labeled with a first label, and with second antibodies having specific binding affinities for member B of the binding pair, wherein the second antibodies are labeled with a second label, to form a second reacted particle, and

d) measuring the first and second labels on the second reacted particle using flow cytometry.

The '003 patent discloses a system for detecting HIV antigen and anti-HIV antibody that includes capturing viral antigen with an immobilized anti-HIV antibody and detecting with a biotin-labeled, human, anti-HIV antibody. A known concentration of viral antigen is added to the patient's sample prior to the assay. A decrease of 30% or more in optical density (OD) from

the OD of the known amount of viral antigen alone was considered antibody positive. A 30% or more increase in OD was considered antigen positive.

The '709 patent discloses a flow cytometry method for analyzing populations of leukocytes that uses two or more fluorescent labels. Leukocytes are identified by combinations of cell surface markers. The combination of the '003 patent and the '709 patent does not teach or suggest a method or kit for simultaneously measuring both members A and B of a binding pair in a biological sample as recited in claims 1-21.

The '003 patent does not teach or suggest that two antibodies, one having specificity for member A and one having specificity for member B, that are differentially labeled can be used to simultaneously detect both members of a binding pair. In contrast, the presence of one of the members of the binding pair is determined indirectly in the '003 patent by spiking the samples with viral antigen and noting if the spiked antigen increases or decreases optical density. Furthermore, the '003 patent does not teach or suggest that both members of a binding pair can be simultaneously measured, wherein the term "measure" refers to both qualitative and quantitative measurements. See, the present specification at, for example, page 6, lines 23-24. The '003 patent refers only to qualitative measurements, i.e., the presence or absence of antigen or antibody. See, for example, column 7, lines 18-22 and column 8, lines 1-6 of the '003 patent, which characterizes samples as positive or negative for HIV antigen and anti-HIV antibody.

The '709 patent does not remedy the deficiencies of the '003 patent as the '709 patent does not teach or suggest that both members of a binding pair can be measured simultaneously. In fact, the '709 patent does not even measure a binding pair. Subpopulations of leukocytes are measured with antibodies that bind to different cell surface markers. Thus, the combination of the '003 patent and the '709 patent does not teach a method or kit for simultaneously measuring both members A and B of a binding pair in a biological sample as recited in claims 1-21. The Examiner is respectfully requested to withdraw the rejection of claims 1-21 under 35 U.S.C. §103.

CONCLUSION

Applicant submits that all of the claims are now in condition for allowance, which action is requested. The Examiner is invited to telephone the undersigned agent if it is felt that such would advance prosecution of the application.

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 7/17/00

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